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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,702	04/15/2002	Camilo Anthony Leo Selwyn Colaco	8830-24	7592

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EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,702	COLACO, CAMILO ANTHONY LEO SELWYN	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *1-7,12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 20040
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment filed 12-1-04 has been entered into the record. Claims 1-13 are pending. Claims 8-11 are under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Applicants should note that the examiner in charge of this Application has changed. Please forward all subsequent papers to Art Unit 1645, Exr. Patricia A. Duffy.

Election/Restrictions

Applicant's election with traverse of Group II in the reply filed on 12-1-04 is acknowledged. The traversal is on the ground(s) that the complexes of Srivastava et al disclose complexes that are constitutive and do not result from stressing a cell.. This is not found persuasive because Srivastava et al teach that "stress protein" as used herein, is understood to mean any cellular protein that satisfies the following criteria. It is a protein whose intracellular concentration increases when a cell is exposed to stressful stimuli, is capable of binding other proteins and peptides, and in capable of releasing the bound proteins or peptides in the presence of adenosine triphosphate or low pH. Stressful stimuli include, but are not limited to heat shock, nutrient deprivation, metabolic disruption, oxygen radicals and infection with intracellular pathogens (column 5, lines 32-42. Therefore the term, stress protein in the claims of Srivastava et al specifically encompass those induced by stressful stimuli including heat shock and infection with intracellular parasites. Applicants argue that their stress-protein complexes are more immunogenic and provide for longer lasting immunity. This is not persuasive to remove an anticipatory reference. Applicants argue Example 4, that shoes that the peptides bound by heat stressed, TNF stress and constiutitve stress protein are significantly different from each other. Applicants are not comparing the antigenic peptides as made by the prior art method with those produced by their method. This is not persuasive because it

is not commensurate with claim 8 and is not free of the art in view of the new art grounds of rejection set forth below. The new art is applied based on Applicants amendments to the claims. The requirement is still deemed proper and is therefore made FINAL.

This application contains claims 1-7 and 12-13 drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Drawings

The drawings in this application are acceptable and have not been objected to by the Draftsperson. No action is required by Applicants in respect to the submitted drawings.

Rejections Withdrawn

The objection to the specification for the typographical errors and the use of trademarks is withdrawn in view of Applicants amendments to the specification.

The request from the previous examiner to update the priority is withdrawn. It is noted that this application was filed under 35 USC 371 and does not claim priority to any previously filed US applications.

The provisional double patenting rejection over 10/049,704 is withdrawn in view of Applicants arguments.

The rejection of claims 8-11 under 35 USC 112, second paragraph is withdrawn in view of the amendments to the claims.

Rejections Maintained

Claims 8-11 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an immunogenic composition comprising a complex of heat shock proteins and antigenic peptides from cells infected with an intracellular

bacteria, parasite or protozoa, it does not reasonably provide enablement for vaccines for reasons made of record in the Office Action mailed 5-27-04.

Applicants argue that additional experimentation does not make the experimentation undue. This is not persuasive, the specification does not teach that the immune response is protective, as is requisite for the term vaccine. It is well established in the immunological arts that antibody response do not correlate with protection from infection. Specifically Chandrashekar et al (US Patent No. 6,248,329) teach at column 1, lines 36-45, that "Although many investigators have tried to develop vaccines based on specific antigens, it is well understood that the ability of an antigen to stimulate antibody production does not necessarily correlate with the ability of the antigen to stimulate an immune response capable of protecting an animal from infection, particularly in the case of parasitic helminthes." Applicants reiterate on pages 13-19 of the response of the teachings of the specification on how to make a vaccine and the components thereof. These teachings were considered, however the statute indicates that the specification needs not only to teach how to make, but how to use. In the instant case, while the process relied upon by Applicants provide for an immunogenic composition (i.e. the ability to make antibody), there is no evidence to show that the antibody is protective. Applicants argue that the composition may have multiple immunogenic components. This is 1- not commensurate in scope with claim 8 and 2- still does not show that the composition produced by the method has the ability to provide for the key issue, a protective response. Applicants argue the predictive value of the animal models for tuberculosis vaccines. It is noted that the instantly claimed vaccine is not tested in any of the requisite animal models and none of the animal models use antibodies as a read-out for protective immunity. The specification does not provide substantive evidence that the claimed vaccines are capable of inducing protective immunity. This demonstration is required for the skilled artisan to be able to use the claimed vaccines for their intended purpose of vaccinating an animal against infection and disease. Without this

demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed compositions. Further, the art is replete with instances where even well characterized antigens that induce an in vitro neutralizing antibody fail to elicit in vivo protective immunity. See Boglesgo et al where a single gonococcal pilin protein fails to elicit protective immunity even though a high level of serum antibody response is induced (page 212, bottom of column 2). The further experimentation is not routine, it is not predictable and the correlation of antibody response to protection from infection is not predictable and such was known in the art at the time of the invention. All Applicants have demonstrated is the production of antibody. Applicants argue their paper (Colaco 2004) indicating that BCG-HspCs protect against live challenge in an animal model and induce T-helper 1 responses. This is not persuasive, the product of the prior art is neither produced by the same method, nor is the composition limited to the composition of the paper. Further, the authors specifically indicate that protection against Mycobacteria is cell mediated. The specification does not provide the necessary correlative immunologic read-out induction of specific cell-mediated immune response. The courts have held that the disclosure is insufficient when testing is necessary to determine the actual use or possible lack of use *(In re Kirk and Petrow* 153 USPQ 48 (CCPA 1967).

Claims 8-11 stand rejected under 35 USC 102(e) as being anticipated by Srivastava et al (US Patent 6,048,530) for reasons made of record in the office action mailed 5-27-04.

Applicants argue the method steps of and the evidence presented in Examples 1-5. This is not persuasive to remove the rejection as applied to claim 8, because it is not commensurate in scope. The claim merely requires one or more complexes. While Applicants examples indicate that the peptide profile produced by a different method are different, there is no showing that any individual HSP-peptide complex as compared to that of the prior art is in fact different. There is overlap between the chromatograms

and there is not showing the compositions of the prior art and that of Examples 1-5 do not have complexes in common, because both are produced by substantially different methods. The claims do not require the entire cell extract and therefore the peptide profile does not distinguish the instant individually claimed one or more complexes, from that of the prior art. Further, the art teaches that regulation of expression of protein in *M. avium* varies according to the mammalian cell bacteria they are exposed to and is influenced by the stage of intracellular infection. Inasmuch as, there is no direct comparison of the composition of the prior art, prepared by a different method using different mammalian cells and conditions, the rejection is maintained.

New Rejections Based on Amendment

Claims 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Srivastava et al (US Patent 6,048,530).

Srivastava et al teach compositions comprising stress protein complexes in pharmaceutically acceptable carriers and adjuvants made by incubating intracellular pathogen in infected cells at 37°C. Srivastava et al differ by not subjecting the mycobacterial infected cells to heat. Srivastava et al teach methods of preparation of HSp70-complexes (columns 13-14). However, Srivastava et al teach that the highly inducible mammalian Hsp70 is hardly detectable at normal temperatures but becomes on of the most actively synthesized proteins in the cell upon heat shock (column 11, lines 24-30).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to modify the method of Srivastava et al by additionally treating the infected cells with heat because Srivastava et al teach that Hsp proteins are induced by heat and the heat treatment would maximize the production of Hsp protein complexes for isolations and purification.

Citation of Relevant Art

Bermudez et al (Immunology and Cell Biology, 75:35-40, 1997) teach that expression of protein in *M. avium* varies according to the mammalian cell bacteria are exposed to and is influenced by the stage of intracellular infection (see page 35, abstract).

Status of Claims

Claims 8-11 stand rejected. Claims 1-7 and 12-13 are withdrawn from consideration.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-Th 6:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patricia A. Duffy
Primary Examiner
Art Unit 1645